INTERNET NEWS

BS. Nguyễn Văn Công

Hypofractionated Radiotherapy For Breast Cancer

- A recent study1 led by Penn's Dr. Justin Bekelman has received wide news coverage,2-4 renewing discussions about the number of radiation treatments needed for some women with breast cancer. In this article, we will review the role of radiotherapy in early stage breast cancer, discuss the evidence for hypofractionated treatment, and examine the study from Bekelman and colleagues.
- What is breast-conserving surgery?
- Many women with early stage breast cancer will be treated with *breast-conserving surgery* (BCS). During BCS, a surgeon cuts out the tumor while leaving the rest of the breast intact. This is different than a mastectomy, where the entire breast is removed.
- What are the benefits of radiotherapy after BCS?
- Although BCS cuts out the visible tumor, it is possible for microscopic cancer cells to be left behind. Radiotherapy—a cancer treatment using high-energy x-rays—can be given after BCS to kill any tumor cells remaining in the breast. The goals of radiotherapy are to prevent the cancer from coming back and, ultimately, to improve survival.
- How much of an impact does radiotherapy have? Consider a woman with early stage breast cancer who undergoes BCS. If no radiotherapy is given, on average the chance of the cancer coming back is 35% and the chance of dying from the cancer is 17% within 10 years. If radiotherapy is given, on average the chance of the cancer coming back is 19% and the chance of dying from the cancer is 14% within 10 years.5 These numbers can be viewed another way. Suppose we treat 100 women with radiotherapy after BCS. The treatment will prevent the cancer from coming back for 18 of those women and it will save 3 of their lives.
- What is fractionation?
- As we discussed before, radiotherapy uses high-energy x-rays to kill tumor cells. A certain total dose of radiation must be delivered for the treatment to be effective. However, it would be too toxic to give this entire dose in a single day. Radiotherapy is therefore *fractionated*, or split up into many smaller daily doses, which add up to the total necessary dose. Standard whole-breast irradiation (WBI) delivers the total dose over 5-7 weeks. *Hypofractionated* WBI delivers the total dose over 3 weeks. In other words, standard fractionation consists of more days with a smaller dose given each day, while hypofractionation consists of fewer days with a slightly larger dose given each day.

- What are the benefits of hypofractionated WBI?
- Because there are fewer days of treatment, hypofractionated WBI is more convenient for patients. It also uses less healthcare resources (i.e. the radiation machine is available to treat other patients). Finally, hypofractionated WBI is not as expensive as standard WBI.
- Is hypofractionated radiotherapy safe and effective?
- Multiple randomized trials comparing hypofractionated WBI to standard WBI have shown no differences between the two approaches over 10 years of follow-up.6-9 Let's look at two of these studies in more detail:
- The Standardisation of Breast Radiotherapy (START-B) trial was performed in the United Kingdom.8 This study randomized 2,215 women to either standard WBI given in 5 weeks or hypofractionated WBI given in 3 weeks. The hypofractionated WBI was shown to be as *effective* as standard WBI (just as likely to prevent cancer from coming back) and as *safe* as standard WBI (not any more likely to cause rib fractures, lung problems, heart problems, or cosmetic changes to the breast) over 10 years of follow-up.
- The Ontario Clinical Oncology Group trial was performed in Canada.9 This study randomized 1,234 women to either standard WBI given in 5 weeks or hypofractionated WBI given in 3 weeks. Similar to the START-B results, the Ontario study showed that hypofractionated WBI was as effective as standard WBI (no differences in cancer coming back and no differences in survival) and as safe as standard WBI (no differences in skin side effects or cosmetic breast outcomes) with 10 years of follow-up.
- Why are some women *not* treated with hypofractionated WBI?
- One concern about hypofractionated WBI is long-term side effects and cosmetic changes to the breast (shrinkage, fibrosis, prominent blood vessels). Remember that the trials discussed above did *not* show any differences in side effects or cosmetic breast changes between hypofractionated WBI or standard WBI over 10 years of follow-up. However, it is possible that after 15 or 20 years there might be a difference. Another important point is that the studies discussed above enrolled a certain type of patient. The majority of women on those trials were over age 50, had tumors smaller than 5 centimeters, had no cancer in their lymph nodes, and did not receive chemotherapy.10 Therefore, for women without these characteristics the evidence for hypofractionated WBI is not as strong.

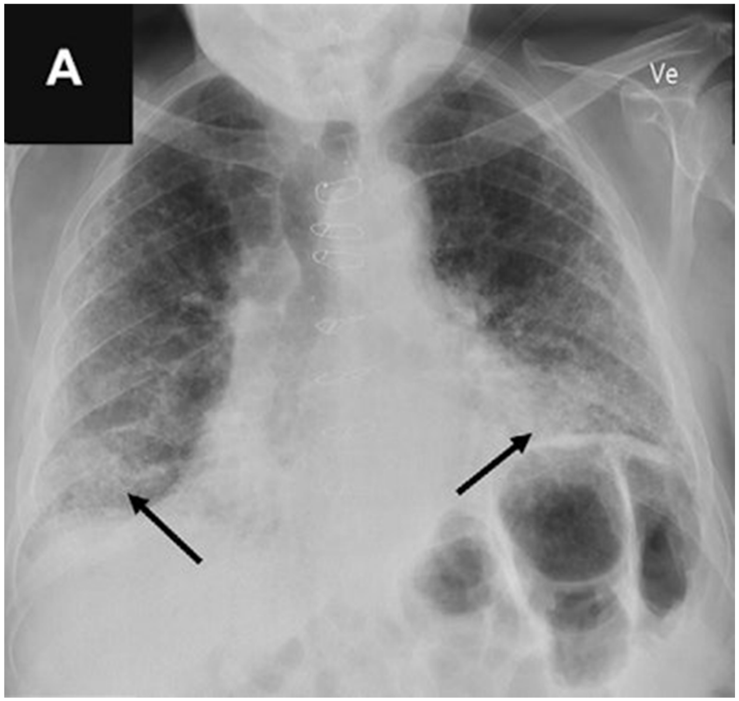
- What questions did the Bekelman study ask?
- The Bekelman study asked two main questions. First, what percentage of women are receiving hypofractionated WBI versus standard WBI? Second, what is the cost of hypofractionated WBI compared to standard WBI?
- Who were the patients in the Bekelman study?
- The authors searched an insurance database containing records of 7.4% of all US women from 2008-2013. They found patients who had breast cancer treated with BCS followed by WBI. Among these patients, the authors then selected those who were older than age 50, had no cancer in the lymph nodes, and had not received chemotherapy. This group of patients was most similar to those women who enrolled in the randomized studies discussed earlier—the studies showing hypofractionated WBI was just as safe and just as effective as standard WBI over 10 years of follow-up.
- What percentage of these women received hypofractionated WBI in the Bekelman study?
- The study found that use of hypofractionated WBI for these women has increased over time. In 2008, 10.6% of these patients received hypofractionated WBI. This number rose to 34.5% in 2013. The remainder of the women received standard WBI.
- What was the cost of hypofractionated and standard WBI in the Bekelman study?
- The average total healthcare costs within 1 year of breast cancer diagnosis were $28,747 for women treated with hypofractionated WBI and $31,641 for women treated with standard WBI. The average radiotherapy-specific costs were $12,622 for women treated with hypofractionated WBI and $16,961 for women treated with standard WBI.
- What were the authors' conclusions?
- The authors quantified the average healthcare savings associated with hypofractionated WBI ($2,894). They also concluded that use of hypofractionated WBI is increasing over time. However, only about 1/3 of women eligible for hypofractionated treatment are currently receiving it—the other 2/3 are getting standard WBI.
- How can I use this information?
- If you or someone you know is at least 50 years old and had early stage breast cancer removed by breast-conserving surgery, you should speak with your radiation oncologist about different options for WBI. You should review both standard WBI and hypofractionated WBI to determine which treatment is right for you.11

CLINICAL NEWS | DIGITAL X-RAY

Radiologists outperform chest x-ray AI

Will Morton
Sep 26, 2023

- Radiologists outperformed four commercially available AI algorithms when diagnosing lung diseases on chest x-rays, with the algorithms limited in complex cases, according to a study published September 26 in *Radiology*.
- The Achille's heel for AI may be its inability to synthesize clinical information radiologists use on a daily basis, such as the patient’s clinical history and previous imaging studies, wrote lead author Louis Plesner, MD, of Herlev and Gentofte Hospital in Copenhagen, Denmark, and colleagues.
- "We speculate that the next generation of AI tools could become significantly more powerful if capable of this synthesis as well, but no such systems exist yet," the group noted.
- While AI tools are increasingly being approved for use in radiological departments, there is an unmet need to further test them in real-life clinical scenarios, according to the authors.
- To that end, in this study, the group compared the performance of four commercially available algorithms – Annalise Enterprise CXR (Annalise.ai), SmartUrgences (Milvue), ChestEye (Oxipit), and AI-Rad Companion (Siemens Healthineers) – compared with the clinical radiology reports of a pool of 72 radiologists. The dataset included 2,040 consecutive adult chest x-rays taken over a two-year period at four Danish hospitals in 2020. The median age of the patient group was 72 years.



A representative posteroanterior chest x-ray (A) in a 71-year-old male patient who underwent examination due to progression of dyspnea shows bilateral fibrosis (arrows), which was misclassified as airspace disease by all four AI tools. Image courtesy of *Radiology*.

Of the sample chest x-rays, 669 (32.8%) had at least one target finding. The chest x-rays were assessed for three common findings: airspace disease, pneumothorax, and pleural effusion.

According to the findings, the AI tools achieved moderate to high sensitivity rates ranging from 72% to 91% for airspace disease, 63% to 90% for pneumothorax, and 62% to 95% for pleural effusion. However, for pneumothorax, for instance, positive predictive values (PPV) for the AI algorithms – the probability that patients with a positive screening test truly have the disease – ranged from between 56% and 86%, compared with 96% for the radiologists, the authors noted.

- PPVs were also lower for the algorithms in airspace disease, with PPVs ranging between 40% and 50%.
- "The AI predicted airspace disease where none was present five to six out of 10 times. You cannot have an AI system working on its own at that rate," Plesner said, in a news release from RSNA.
- Plesner noted that most studies generally tend to evaluate the ability of AI to determine the presence or absence of a single disease, which is a much easier task than real-life scenarios where patients often present with multiple diseases.
- "In many prior studies claiming AI superiority over radiologists, the radiologists reviewed only the image without access to the patient’s clinical history and previous imaging studies. In everyday practice, a radiologist’s interpretation of an imaging exam is a synthesis of these three data points," he said.
- Ultimately, current commercially available AI algorithms for interpreting chest x-rays don't appear to be ready for making autonomous diagnoses, but they may be useful as tools for boosting radiologists’ confidence in their diagnoses by providing a second look, the researchers added.
- "Future studies could focus on prospective assessment of the clinical consequence of using AI for chest radiography in patient-related outcomes," the group concluded.

CLINICAL NEWS | ULTRASOUND

Ultrasound nomogram performs well on soft-tissue tumors

Amerigo Allegretto
Sep 12, 2023

Combining ultrasound imaging and clinical features can help radiologists identify malignant soft-tissue tumors for radiologists, suggest findings published September 11 in *Ultrasound in Medicine & Biology*. Researchers led by Yusen Zhang from Peking University Shenzhen Hospital in China found that a model combining these features achieved high diagnostic performance in evaluating these tumors compared with using imaging features alone.

"The diagnostic model also had superior accuracy compared with the performance of radiologists, suggesting its potential in aiding radiologists in clinical decision-making in patients with soft-tissue tumors," Zhang and colleagues wrote.
Ultrasound is the go-to imaging modality for assessing soft-tissue tumors due to its convenience and safety. With recent advancements such as color Doppler and high-frequency imaging, ultrasound also shows high resolution of superficial soft tissues.

However, the researchers noted that even with these advancements, it's still a challenge for radiologists to diagnose soft-tissue tumors with imaging or clinical information alone. They also pointed out interobserver variability and operator dependence of ultrasound as hindrances to the technology's diagnostic performance. Zhang et al sought to test the performance of a diagnostic nomogram that incorporates both ultrasound and clinical features to differentiate between malignant and benign soft-tissue tumors. The team developed two models for its study: One blended clinical and ultrasonic features, and the other used ultrasonic features only. Clinical variables used for the combined model included patient age, tumor history, tumor location, size, boundaries, internal echogenicity, posterior acoustic changes, and blood flow patterns.

- The nomograms were tested on soft-tissue tumors from various areas of the body, including the head and neck, and upper and lower extremities. Also, tumors came from the skin, subcutaneous, and muscular layers, as well as in the bone.
- For the study, the authors included 613 patients with 195 malignant and 418 benign soft-tissue tumors. They also compared the performance of the models to each other, as well as that of two radiologists. They found that the nomogram that used both ultrasonic and clinical features had the highest diagnostic performance of the three methods.

Comparison between nomograms, radiologists				
Measure	Radiologists (average)	Ultrasound-only model	Ultrasound-clinical features model	p-value
Area under the curve (AUC)	0.81	0.89	0.95	< 0.001 (for both)

The researchers also evaluated the integrated discrimination improvement (IDI) for both nomograms. This measure reflects how the new model increases risk in events and decreases risk in non-events. The team found that the IDI between the two nomograms was 0.15 ($p < 0.001$), which it wrote suggested that accuracy was improved by adding clinical features.

Zhang et al wrote that they expect that the combined model may provide a reference for radiologists in classifying soft-tissue tumors that are hard to diagnose. They added that the nomogram could help reduce missed diagnoses of malignancies, as well as unnecessary biopsies.

They also called for future studies to use prospective multicenter database collection to validate the model's performance and include novel ultrasound techniques and patient follow-up to predict prognosis.

"Given the consistency of the model in variable inclusion with previous studies, we believe that the model has relatively high stability but might still be influenced by the constitution of the pathological types of soft-tissue tumors in the study population," they concluded.

CLINICAL NEWS | DIGITAL X-RAY

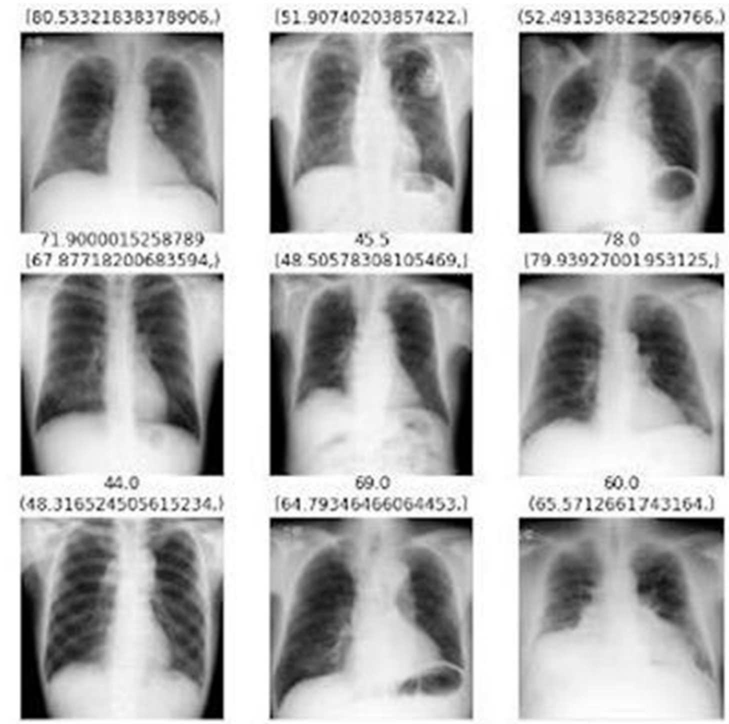
X-ray-based AI can help identify malnourished bedridden patients

Will Morton
Sep 11, 2023

AI can accurately glean height and weight from chest x-rays -- a task that could help clinicians implement rapid nutritional interventions for bedridden patients, according to a group in Nagasaki, Japan.

A team led by Yasuhiko Nakao, MD, PhD, of Nagasaki University, developed a convolutional neural network to predict the height and weight of patients based on more than 14,000 x-rays acquired over a 15-year period. The model's predictions had a high correlation with actual height and weight -- key information for proper nutritional assessment, they wrote.

"Our chest radiographic prediction model has a high correlation with actual height and weight and can be combined with clinical nutrition factor information for rapid assessment of risk for malnutrition," the group noted in a study published September 6 in *Clinical Nutrition Open Science*.



Current guidelines recommend prompt nutrition intervention and initiation of nutrition therapy within 24 to 48 hours of admission in patients suspected of malnutrition, the authors explained. To determine a patient's metabolic rate and nutrition needs, clinicians use a formula called the Harris-Benedict equation, which requires patients' age, gender, height, and weight. However, determining height and weight can be difficult in patients with serious infections, those in intensive care units, and in bedridden elderly patients with severe contractures, they wrote.

In this study, the researchers aimed to develop a convolutional neural network (CNN) model that could potentially assess height and weight based on chest x-rays. They used 6,453 x-rays from male patients and 7,879 x-rays from female patients to train and test the model, with height and weight data extracted from electronic medical records, then applied an image regression model (ResNet-152) that previously has been reported to predict age from CT imaging data. For input, they prepared linked datasets in which the CNN associated the x-rays with height and weight.

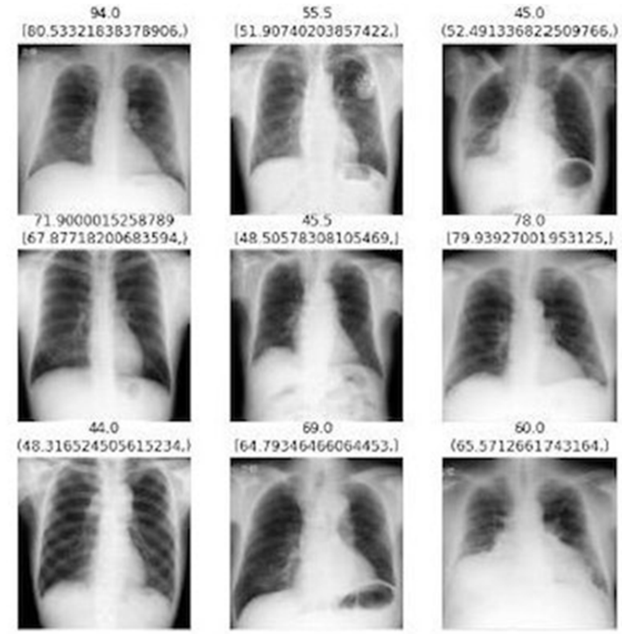
The team based its statistical analysis on the comparison of the model's predictions against the original height and weight values using Pearson's correlation coefficients. According to the findings, the correlations between the model's predicted values and actual values for males and females were 0.855 and 0.81, while the correlation coefficients for weight for males and females were 0.793 and 0.86.

"Our chest radiographic prediction model has a high correlation with actual height and weight and can be combined with clinical nutrition factor information for rapid assessment of risk for malnutrition," the group wrote.

Ultimately, determining the height and weight of bedridden patients in emergency departments may be delayed during times of high hospital admissions, such as the COVID-19 pandemic, the authors noted. These information delays could be reduced using their model, they suggested.

Also, since the model was developed using standing chest x-rays for which actual height data existed, the authors plan a prospective study in the future comparing the model's rates of agreement based on supine x-rays, they added.

"Importantly, our model is an illustration of the potential of automated imaging AI for proper nutrition prediction models in elderly patients," the researchers concluded.



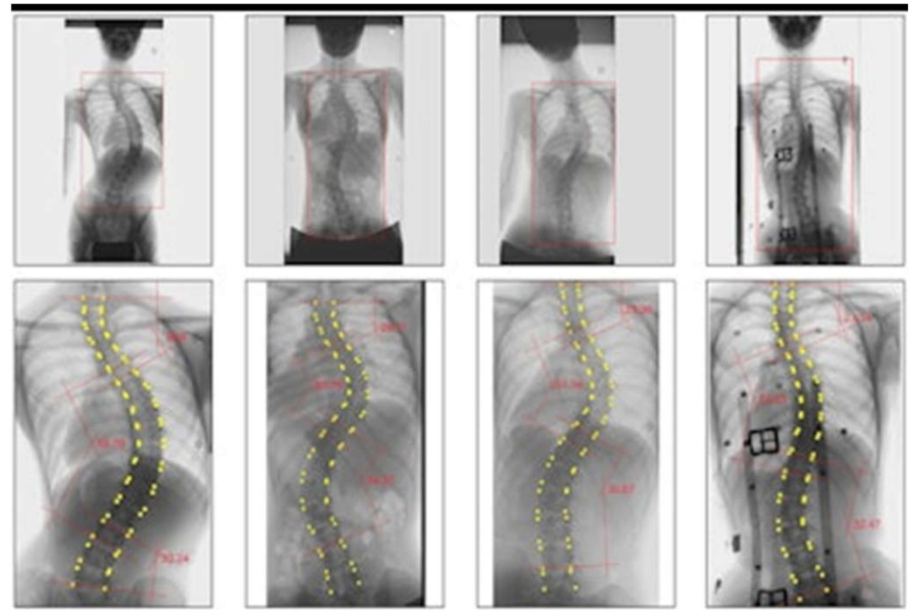
A representative set of chest x-rays of male patients, with the numbers on the top of each image representing the actual and computed heights (in parentheses). Image courtesy of Clinical Nutrition Open Science through CC BY 4.0.

IMAGING INFORMATICS | ARTIFICIAL INTELLIGENCE

AI shows promise for evaluating scoliosis on spine x-rays

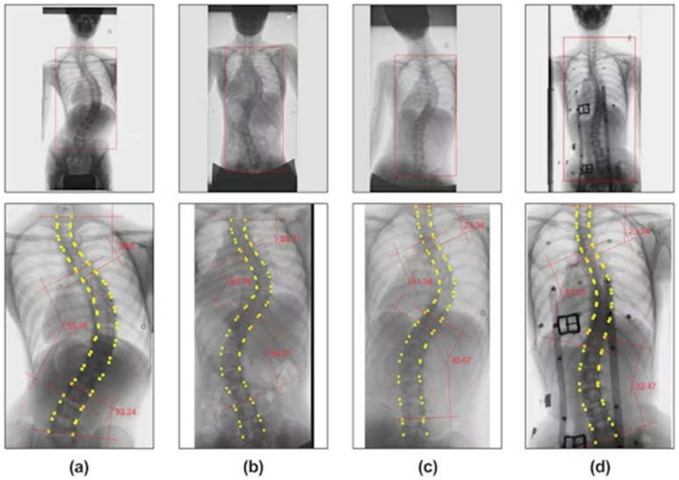
Will Morton

Orthopedic surgeons in Japan have developed an AI method based on spine x-rays that could be used to help evaluate scoliosis, according to a study published September 4 in *Scientific Reports*.
A team led by Yoshihiro Maeda, PhD, of Keio University in Tokyo, trained a deep-learning algorithm to detect vertebrae and automatically measure spine curves on x-ray images of patients with adolescent idiopathic scoliosis (AIS). In testing, the method compared well with evaluations by expert doctors, they found.



"The proposed method showed a high correlation with the doctors' measurements, regardless of the [Cobb angle] size, doctors' experience, and patient posture," the group wrote.
Children between 10 and 17 years old who have scoliosis of unknown cause are classified as having AIS, with standing whole-spine x-ray as the standard diagnostic imaging technique. Surgery is typically based on the severity of the spinal deformity, which is indicated by the Cobb angle, a measurement between the two lines of the vertebral endplates at the upper and lower ends of the curve.
Years ago, doctors measured Cobb angles to diagnose scoliosis using a protractor on printed x-ray images, with scoliosis considered mild with a Cobb angle less than 20° and severe with Cobb angles greater than 50°. Most PACS now have built-in features that automatically calculate the angle, yet PACS still require manual selection of the appropriate end vertebrae by surgeons, the researchers noted.

- As a potential aid in these cases, the researchers aimed to train and evaluate a convolutional neural network (CNN) that can automatically measure the Cobb angle.
- In training, they used 1,021 full-length x-ray images of the spines of patients with AIS taken between 2009 and 2020. The data included supine position, supine side-bending, and wearing-brace images in addition to the standing images, as their aim was to ensure that the proposed algorithm was not limited to patients in the standing position, they wrote.
- Essentially, the CNN operates in three stages, the authors explained. In the first stage, it identifies the region of interest (ROI), which includes the whole spine with 12 thoracic and five lumbar vertebrae. In the second stage, the four corners of each vertebra are detected as feature points and in the final stage, the model uses the 17 detected feature points to measure the major and minor curves of the Cobb angle.
- In a separate set of 155 images from patients with AIS, the algorithm's performance was compared with the performance of six doctors with different levels of experience (two experts who specialize in scoliosis treatment, two intermediates who were spine specialists, and two novices who were doctors in their third year of postgraduate studies).



Results of Cobb angle measurements using the proposed method. The upper row shows the detected region of interest (indicated by a rectangle on the image) and the lower row shows the Cobb angle measurement results. Each column shows examples of (a) standing, (b) supine, (c) bending, and (d) wearing-brace x-ray images. Image courtesy of Scientific Reports through CC BY 4.0.

Three curves were evaluated at the upper, middle, and lower parts of the spine, which they classified as major (largest), minor 1 (next largest), and minor 2 (smallest) curves. Reliability was determined by calculating differences in the Cobb angle measurements by the doctors and the AI using intraclass correlation coefficients (ICCs).

The average Cobb angle difference ranged from approximately from 2.8° to 4.6°, with the largest difference between the doctors' manual average Cobb angle and the AI average Cobb angle being 4.6° at the minor 2 region with patients in a bending position, according to the findings.

Overall, the ICCs recorded for the six doctors and AI were excellent or good, with a value of 0.973 for the major curve in the standing position, the researchers wrote.

"The mean error between AI and doctors was not affected by the angle size, with AI tending to measure 1.7°-2.2° smaller than that measured by the doctors," the authors wrote.

Ultimately, since AIS progresses gradually with growth, it is important not to miss the curve in the early stages of the disease, the researchers noted. Therefore, the ability to detect even small angles may be useful in screening for AIS, they wrote.

Moreover, the total computation time for the AI is a few seconds per case and this could save time and reduce the burden on physicians in medical settings where a huge number of scoliosis measurements are required, according to the researchers.

"The proposed method showed excellent reliability, indicating that it is a promising automated method for measuring [Cobb angle] in patients with AIS," the group concluded.

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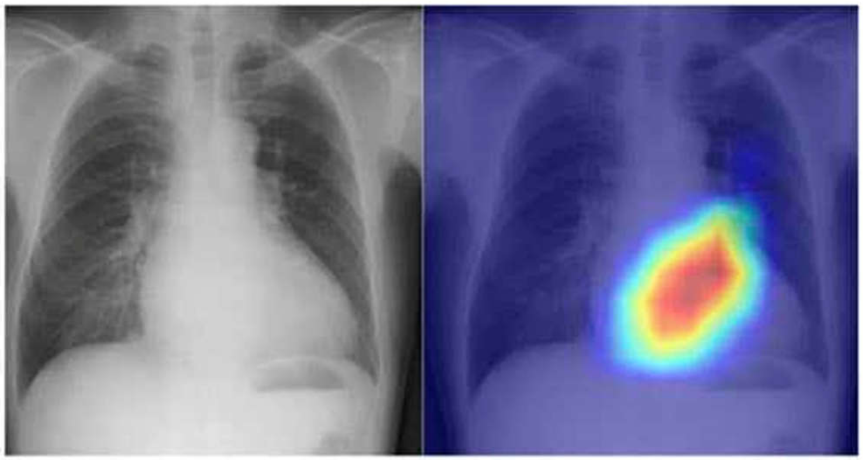


Groundbreaking AI-Based Method Accurately Classifies Cardiac Disease Using Chest X-Rays

Groundbreaking AI-Based Method Accurately Classifies Cardiac Disease Using Chest X-Rays

Valvular heart disease, a leading cause of heart failure, is commonly diagnosed using echocardiography. However, this technique demands specialized expertise, leading to a shortage of proficient technicians. Chest radiography, on the other hand, is a widely used diagnostic method for identifying primarily lung diseases. Even though the heart is visible in chest radiographs or chest X-rays, its potential to detect cardiac function or disease has been largely unexplored until now. Given their widespread use, rapid execution, and high reproducibility, chest X-rays could serve as a supplementary tool to echocardiography for diagnosing cardiac conditions if they could accurately determine cardiac function and disease. Now, an innovative artificial intelligence (AI) tool uses chest X-rays to classify cardiac functions and identify valvular heart disease with unprecedented accuracy.

Scientists at Osaka Metropolitan University (Osaka, Japan; www.omu.ac.jp) have developed an AI-based model capable of accurately classifying cardiac functions and diagnosing valvular heart diseases using chest X-rays. Given the potential for bias and resultant low accuracy if AI is trained on a single dataset, the team collected a multi-institutional dataset comprising 22,551 chest X-rays and corresponding echocardiograms from 16,946 patients across four facilities between 2013 and 2021. The AI model was trained using chest X-rays as input data and the corresponding echocardiograms as output data, enabling it to learn the features connecting the two datasets.

The AI model succeeded in precisely classifying six selected types of valvular heart disease, with the Area Under the Curve (AUC is a rating index denoting an AI model's capability with a value range from 0 to 1—the closer to 1, the better) ranging from 0.83 to 0.92. The AUC was 0.92 at a 40% cut-off for detecting left ventricular ejection fraction—an essential metric for monitoring cardiac function.

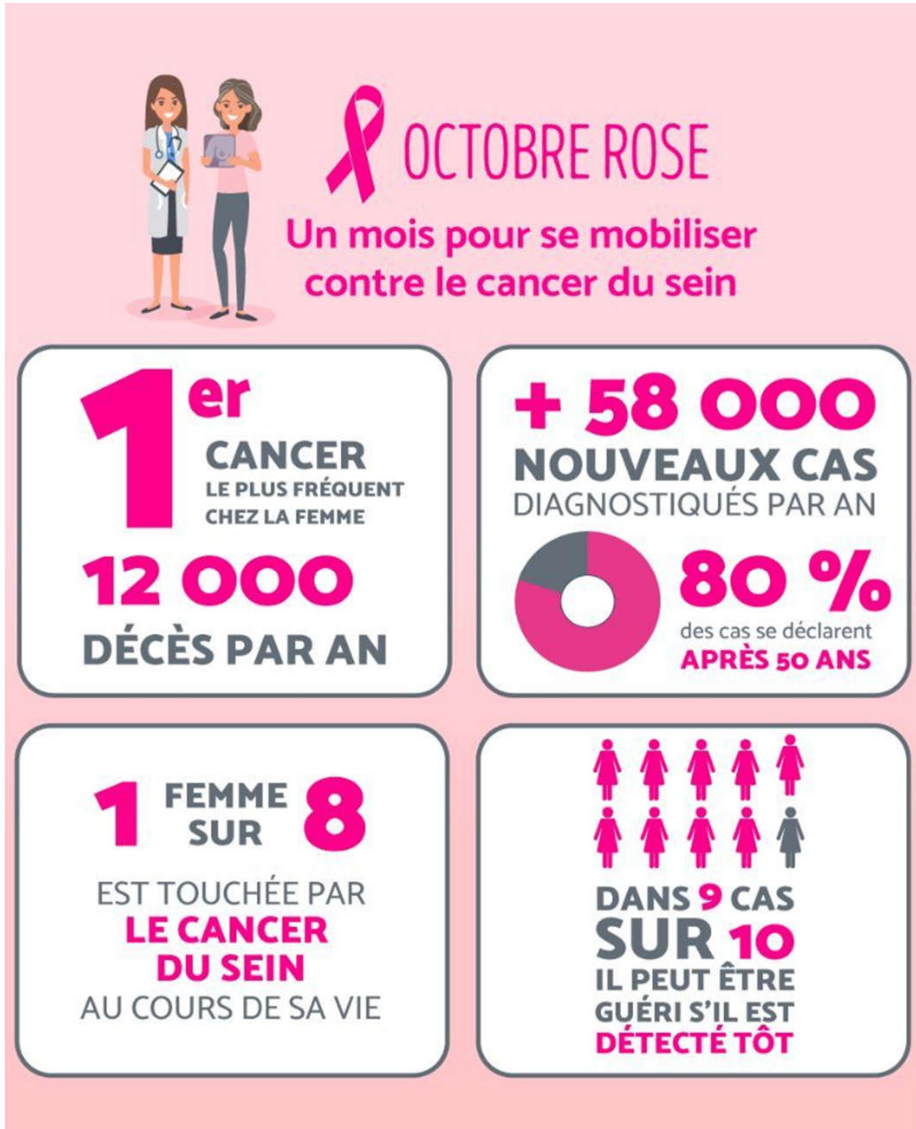
"It took us a very long time to get to these results, but I believe this is significant research," stated Dr. Daiju Ueda from Osaka Metropolitan University who led the research team. "In addition to improving the efficiency of doctors' diagnoses, the system might also be used in areas where there are no specialists, in night-time emergencies, and for patients who have difficulty undergoing echocardiography."

Image: An artificial intelligence-based model classifies cardiac functions from chest radiographs (Photo courtesy of Osaka Metropolitan University)

First-of-Its-Kind Technology Detects 'Invisible' Risk of Heart Disease from Routine Cardiac CT Scans

Coronary Artery Disease (CAD), the leading cause of death globally, often remains undetected until it's too late. For many years, cardiologists have understood that inflammation is a key factor driving the onset of CAD and plaque rupture. However, existing diagnostic tests do not

Caristo Diagnostics' (Oxford, UK; www.caristo.com) CaRi-Heart technology can detect coronary inflammation as well as atherosclerosis (plaque) using standard cardiac CT scans. The CaRi-Heart report quantifies coronary inflammation through a unique and patented biomarker called the Fat Attenuation



OCTOBRE ROSE
Un mois pour se mobiliser
contre le cancer du sein
1er CANCER
LE PLUS FRÉQUENT
CHEZ LA FEMME
12 000
DÉCÈS PAR AN
+ 58 000
NOUVEAUX CAS
DIAGNOSTIQUÉS PAR AN
80 %
des cas se déclarent
APRÈS 50 ANS
1 FEMME SUR 8
EST TOUCHÉE PAR
LE CANCER
DU SEIN
AU COURS DE SA VIE
DANS 9 CAS
SUR 10
IL PEUT ÊTRE
GUÉRI S'IL EST
DÉTECTÉ TÔT